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Evaluation of solid tumors in the first year of life: A single-center 30-year experience

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Abstract

Aim: The diagnosis, treatment, and follow-up of infantile tumors are of special importance among all pediatric malignancies. Here in this study, we aimed to evaluate the demographic, clinical, pathological, and surgical properties of infantile tumors followed by our department.

Material and Methods: We evaluated 78 cases of infantile tumors <12 months of age who were registered in Gazi University, Faculty of Medicine, Department of Pediatric Oncology between 1991-2021.

Results: Infantile tumors account for 6.8% of all pediatric malignancies followed by our department. There were 38 girls and 40 boys whose mean age was 186.60±110 days (8 -350 days). Nine of our patients were diagnosed during the neonatal period. The most common tumor was neuroblastoma in 24 patients (30.7%) while the second most common tumor was central system tumor in 13 cases (16.6%). Other tumors included 10 mature/ immature teratomas, 8 renal tumors (10.2%), 6 retinoblastomas (7.6%), 6 liver tumors (7.6%) and soft tissue sarcoma in 6 patients, yolk sac tumors (3.8%), and Langerhans cell histiocytosis (2.5%). Fifty-one patients (65.3%) received chemotherapy, 19.4% received radiotherapy and 86.6% had surgical resection for treatment modalities. Total surgical resection has been applied to 67.2% of patients. Relapses were observed in 23 patients (29.4%), most commonly at the site of the primary tumor. Forty-four patients are alive without disease, 9 patients were lost to follow-up, and 25 patients died. The follow-up period of the patients ranged from 4 months to15 years. Overall survival was 67% and event-free survival was 58%.

Discussion: In our study, neuroblastoma was the most common solid tumor seen in the infantile period, consistent with the literature. With intensive treatment modalities and awareness of treatment-related toxicities for solid tumors of the infantile period, long-term survival can be achieved.

Keywords
Solid Tumors, Infant, Newborn

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Introduction

Cancer is an important life-threatening disease in childhood, as in any age group. Although childhood cancer is a rare and fatal disease, with increased treatment options, survival rates can increase to approximately 70% [1,2]. The newborn and the first year of life, when physical and mental growth is the fastest, are very important periods of childhood. It has been reported in the literature that neonatal tumors constitute 2% of all childhood malignancies, and infant tumors (under 1 year of age) constitute 10% of childhood cancers [3-5]. The histopathological features, treatment approaches, prognosis, and toxicity of infant tumors vary from childhood. Retinoblastoma, neuroblastoma, germ cell tumors, Wilms tumors, and hepatoblastoma are reported in the literature as the most common solid tumors under 1 year of age [6,7]. Cancer treatment may require a multidisciplinary approach consisting of surgery, radiotherapy, and chemotherapy. However, treatment modalities can cause serious toxicity, morbidity, and mortality in newborns and infants who are growing and developing physically and mentally [8,9]. Surgery, which must be performed on a small area without damaging normal tissue, is quite difficult. Radiotherapy is rarely administered due to its serious toxicity. Dose reductions are made in chemotherapy protocols all over the world due to tissue and organ immaturity and sensitivity to chemotherapeutics during the neonatal and infant periods. Patients need to be regularly followed up for many years in terms of side effects that may develop due to the treatments [10,11].

In this study, we aimed to increase awareness of tumors in the first year of life and evaluate the demographic, clinical, pathological characteristics, treatment properties, and toxicities of less than one year old followed in our department. It was planned to compare the results of our center with the literature.

Material and Methods

We retrospectively evaluated 78 cases of infantile tumors <12 months of age who were registered at Gazi University, Faculty of Medicine, Department of Pediatric Oncology between 1991-2021. Patient age, gender, histopathological diagnosis, treatment used, and toxicities were evaluated. It was evaluated whether patients diagnosed in the neonatal period had an antenatal diagnosis. The localization of the tumor, the presence of metastases, and the treatment outcomes were recorded. Patients with leukemia were not included in this study. This study was approved by the Ethics Committee of Gazi University (No.2023-1100).

Statistical analysis

Quantitative data were represented by mean ± standard deviation. Percentages described qualitative data and the comparison of these data was performed using the Chi-square test. Patient and disease characteristics were compared between groups using the Mann-Whitney U and Chi-square/ Fisher tests for numerical and categorical variables, respectively.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

Infantile tumors account for 6.8% of all pediatric malignancies followed by our pediatric oncology department. There were 38 girls and 40 boys whose mean age was 186.60±110 days (8 -350 days). Nine out of 78 patients were diagnosed during the neonatal period. The most common tumor was neuroblastoma in 24 patients (30.7%), while the second most common tumor was a central system tumor in 13 cases (16.6%), and extracranial germ cell tumors in 13 patients. Table 1 shows the distribution of tumors according to their histopathological diagnosis.

When patients with neuroblastoma were evaluated, 2 patients were diagnosed during antenatal examination. Five patients had findings of spinal cord compression, and the other patients with neuroblastoma presented with an abdominal mass in this study. Clinical and radiological follow-up was carried out for the patient diagnosed during the antenatal period. Histopathological diagnoses of all other patients were confirmed by biopsy/surgery as neuroblastoma. Brain tumors presented with symptoms such as vomiting, afebrile seizures, increased head circumference, and cranial nerve paralysis. All patients underwent cranial CT/MRI imaging and surgical treatment. Patients with retinoblastoma presented with symptoms of strabismus and leukocoria. All patients were diagnosed by eye examinations performed under general anesthesia. All patients with retinoblastoma were considered hereditary cases, and

Table 1. Distribution of solid tumors in the first year of life

Characteristics	Number of patients, n (%)
Sex	
Male	40 (51.2)
Female	38 (48.7)
Diagnosis	
● Neuroblastoma	24 (30.7)
● Central nervous system tumors	13 (16.6)
✓ Embryonal tumors	9 (11.5)
- Medulloblastoma	2 (2.5)
-Atypical teratoid/rhabdoid tumor	5 (6.4)
-Supratentorial primitive neuroectodermal tumor	2 (2.5)
✓ Choroid plexus neoplasms	4 (5.1)
● Extracranial germ cell tumor	13 (16.6)
✓ Mature teratoma	8 (10.2)
✓ Immature teratoma	2 (2.5)
✓ Malignant germ cell tumors (yolk sac tumor)	3 (3.8)
-Sacrococcygeal/retroperitoneal	2 (2.5)
-Testicular	1 (1.2)
● Renal tumors	8 (10.2)
✓ Wilms tumor	4 (5.1)
✓ Congenital mesoblastic nephroma	3 (3.8)
✓ Malignant Rhabdoid tumor	1 (1.2)
● Retinoblastoma	6 (7.6)
● Liver tumors	6 (7.6)
✓ Hepatoblastoma	4 (5.1)
✓ Hemangioendothelioma	2 (2.5)
● Soft tissue sarcoma	6 (7.6)
✓ Rhabdomyosarcoma	2 (2.5)
✓ Infantile fibrosarcoma	1 (1.2)
✓ Infantile inflammatory myofibroblastic tumor	2 (2.5)
✓ Hemangiopericytoma	1 (1.2)
● Histiocytic Disease	2 (2.5)
✓ Langerhans cell histiocytosis	2 (2.5)

Table 2. Treatment modalities and final conditions of the patients

Disease Number of patients, (N)	Chemotherapy	Surgery	Radiotherapy	Lost of follow-up	Exitus	Remission
Neuroblastoma N=24	22	20	8	4	8	12
Central nervous system tumors N=13	7	13	-	2	9	2
Extracranial germ cell tumor N=13	3	13	1	-	-	13
Renal tumors N=8	5	8	3	0	1	7
Retinoblastoma N=6	4	3	-	1	2	3
Liver tumors N=6	5	4	1	1	2	3
Soft tissue sarcoma N=6	5	6	2	1	3	2

three patients had bilateral tumors. One out of these 3 patients had a pineal mass and the patient was diagnosed with trilateral retinoblastoma.

Catecholamines were elevated in urine in 17 patients out of 24 patients with neuroblastoma. As serum tumor markers, alpha-fetoprotein (AFP) values were detected for all patients diagnosed with germ cell tumors. Six out of 10 patients diagnosed with mature teratoma were in the first 3 months of life, the mass originated from the sacrococcygeal region and had very high AFP values. AFP values of all patients diagnosed with yolk sac tumors (sacrococcygeal/retroperitoneal, and ovarian/testicular) were very elevated. In this study, normal AFP values were found in only 2 patients, a 9-month-old and an 11-month-old patient with mature teratoma located in the sacrococcygeal region.

When solid tumors were staged, 8 patients had metastatic and 2 patients were diagnosed as stage 4S in 24 patients with neuroblastoma. Two patients out of 13 cranial tumors of patients had spinal metastatic involvement at diagnosis. The histopathological diagnoses of these patients were choroid plexus carcinoma in one patient and the other patient was medulloblastoma in our series.

Surgical and chemotherapy treatments were applied in accordance with the histopathological diagnoses of the patients in this study. Fifty-one patients (65.3%) received chemotherapy, 15 patients (19.4%) received radiotherapy and 67 patients (86.6%) had surgical resection for treatment modalities. Total surgical resection has been applied to 45 patients (67.2%) out of 67 patients who had surgical resection. No patient received craniospinal radiotherapy. Low-dose radiotherapy was applied to patients with neuroblastoma and Wilms tumor according to oncological guidelines such as stage, presence of anaplasia in the tumor, surgical margin, and surgical rupture status. Treatment modalities and final conditions of the patients are listed in Table 2.

Chemotherapy-related side effects were observed febrile neutropenia (n=42), erythrocyte and platelet replacement requirement (n=29), anaphylaxis (n=1), afebrile convulsion (n=1), electrolyte disorders such as hyponatremia (n=7), and hypocalcemia (n=5).

In our series, 23 patients had relapses (29.4%), most commonly in the primary tumor site. Forty-four patients are alive without disease, 9 patients were lost to follow-up, and 25 patients died. The follow-up period of the patients ranged from 4 months to 15 years. Overall survival was 67% and event-free survival was 58%.

Discussion

Solid tumors of the infant and neonatal periods are not common, but they may differ from other childhood age groups in terms of management and treatment strategies [9,11]. Although the incidence of tumors in infancy varies according to centers, it has been reported to be between 2%-14% in the literature [3-5]. Das et al. [7] reported an incidence of infantile tumors of 5.7% in their large series consisting of 266 patients. In our study, we found that the incidence of solid tumors was 6.8% in the first year of life. It was similar to the literature.

Leukemia, retinoblastoma, neuroblastoma, central nervous system (CNS) tumors, germ cell tumors, Wilms tumors, and hepatoblastoma are reported in the literature as the most common solid tumors under 1 year of age [11,12]. Lymphomas were the second most common childhood tumors in developing countries [4]. But in our series, we have not seen any infant having lymphoma. Despite acute leukemia is the most common malignancy in childhood, leukemia cases have not been included because we do not follow up leukemia in our pediatric oncology department. In our study, we found neuroblastoma (30%) as the most common solid tumor less than 1 year of age. Bhatnagar [3] pointed out that neuroblastoma was the most common solid tumor with a rate of 22% in 59 infant cases, and Das et al. [7] found that neuroblastoma was the most common solid tumor with a rate of 18.7% in 266 infant patients. CNS tumors were the second most common childhood malignancy in Western countries [7]. CNS tumors were the second most common malignancy in our series, since we are a referral center for pediatric neurosurgery.

When assessing tumor markers, almost all neuroblastomas are known to produce catecholamines such as vanillylmandelic acid (VMA) and homovanillic acid (HVA). Alpha-fetoprotein (AFP) as a serum tumor marker aids in the diagnosis of yolk sac tumors. Because of the wide variation in levels at birth, especially with infants of less than 40 weeks gestational age, and the wide variability in half-life at different ages within the first year of life, difficulties arise in interpreting both the absolute level of AFP in the first year of life and the decay of serum AFP as an indication of yolk sac tumors in infants younger than 8 months [13,14]. Therefore, 6 out of 10 patients diagnosed with mature teratoma were in the first 3 months of life, the mass originated from the sacrococcygeal region and had very high AFP values.

Treatment of cancer in infants and the neonatal period may require a multidisciplinary approach consisting of surgery, radiotherapy, and chemotherapy [9,14]. The histopathology of

the tumor is important in the choice of treatment for solid tumors. Since most childhood malignant tumors are chemosensitive, complete recovery can be achieved with rapid and appropriate treatment of the malignancy in pediatric cancer patients [8,11]. But, the treatments have caused serious toxicity, morbidity, and mortality in the first year of life [7,15]. Tissue immaturity, small body proportion, low body weight cause difficulty in surgery and chemotherapy during the neonatal and infant period [16,17]. However, remission without sequela can be achieved with early diagnosis in the first life of tumors such as soft tissue masses, liver tumors, and retinoblastoma [12,18,19]. It is necessary to prevent the side effects of chemotherapy and tissue deformities caused by surgery in infants and newborns who are in a period of rapid neurological and physical growth [11,17,20]. Also, we also would like to emphasize that detailed examination such as abdominal, cardiac and neurological examination, presence of hepatosplenomegaly, head circumference measurement, and examination of extremities are important for early diagnosis.

Conclusion

In our study, neuroblastoma was the most common solid tumor seen in the first year of life, consistent with the literature. Early diagnosis, with intensive treatment modalities and awareness of treatment-related toxicities for solid tumors of the infantile period, long-term survival can be achieved.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

References

1. Jin M, Tian Z, Xie Y, Zhang Z, Li M, Yu Y, et al. Diagnosis and treatment of infantile malignant solid tumors in Beijing, China: A multicenter 10-year retrospective study. Pediatr Investig. 2020;4(3):178-85.

2. Davenport KP, Blanco FC, Sandler AD. Pediatric malignancies: neuroblastoma, Wilm's tumor, hepatoblastoma, rhabdomyosarcoma, and sacroccygeal teratoma. Surg Clin North Am. 2012;92(3):745-67.

3. Zhi T, Zhang WL, Zhang Y, Wang YZ, Huang DS. Prevalence, clinical features and prognosis of malignant solid tumors in infants: a 14-year study. Bosn J Basic Med Sci. 2021;21(5):598-606.

4. Bhatnagar SN. An audit of malignant solid tumors in infants and neonates. Neonatal Surg. 2012;1(1):5.

5. Yang CP, Hung IJ, Jaing TH. Cancer in infants: a review of 82 cases. Pediatr Hematol Oncol. 2005; 22(6):463-81.

6. Zhu L, Chen G, Shen Y, Wang X, Gao L, Zhao Y, et al. Infantile synchronous primary bilateral testicular germ cell tumor: a case report and review of the literature. Transl Androl Urol. 2019;8(5):540-7.

7. Das U, Appaji L, Kumari BS, Lakshmaiah KC, Padma M, Kavitha S, et al. A single center experience in 266 patients of infantile malignancies. Pediatr Hematol Oncol. 2014;31(6):489-97.

8. Jauquier N, English N, Davidson A, Cox SG. Solid malignancies during the first year of life: A 20-year review at Red Cross War Memorial Children's Hospital, Cape Town, South Africa. S Afr Med J. 2022;112(6):418-25.

9. Toescu SM, James G, Phipps K, Jeelani O, Thompson D, Hayward R, et al. Intracranial neoplasms in the first year of life: Results of a third cohort of patients from a single institution. Neurosurgery. 2019; 84:636-46.

10. Desandes E, Faure L, Guissou S, Goujon S, Berger C, Minard-Colin V, et al. Infant cancers in France: Incidence and survival (2000–2014). Cancer Epidemiol. 2020; 65:101697.

11. Allen-Rhoades W, Whittle SB, Rainusso N. Pediatric Solid Tumors of Infancy: An Overview. Pediatr Rev. 2018; 39(2):57-67.

12. Jin M, Zhao J, Zhang D, Zhang C, Zhao W, Wang X, et al. Analysis of the short-term curative effect of 356 cases of intraocular retinoblastoma in children. Pediatr Investig. 2018; 2(4):236-41.

13. Pizzo PA, Poplack DG, editors. Principles and Practıce of Pediatric Oncology. Philadelphia: Wolters Kluwer; 2016. p.900-10.

14. Chandrasekaran A. Neonatal solid tumors. Pediatr Neonatol. 2018; 59(1):65-70.

15. Hadley G.P, Govender D, Landers G. Malignant solid tumors in neonates: an African perspective. Pediatr Surg Int 2002; 18: 653-7.

16. Albert A, Cruz O, Montaner A, Vela A, Badosa J, Castañón M, et al. Congenital solid tumors. A thirteen-year review. Cir Pediatr. 2004;17(3):133-6.

17. Isaacs H Jr. Fetal and neonatal hepatic tumors. J Pediatr Surg. 2007; 42(11):1797-803.

18. López AR, Villafruela AC, Rodríguez LJ, Doménech ME. Neo¬natal neoplasms: a single-centre experience. Ann Pe¬diatr (Barc) 2006; 65(6):529-35.

19. Kim SH, Cho YH, Kim HY. Two Cases of Infantile Intra-abdominal Inflammatory Myofibroblastic Tumor. Pediatr Gastroenterol Hepatol Nutr. 2014;17(2):116-20.

20. Mizia-Malarz A, Sobol-Milejska G, Buchwald J, Woś H. Inflammatory Myofibroblastic Tumor of the Heart in the Infant: Review of the Literature. J Pediatr Hematol Oncol. 2016; 38(8):298-302.

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